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MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,260	ELLIOTT ET AL.	
	Examiner	Art Unit	
	Fozia M Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *9,12-42,46-55 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11,43-45,56 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence alignment*.

DETAILED ACTION

Election/Restriction:

1a. Applicant's election of the invention of Group I (claims 1-8, 10, 11, 43-45, 56 and 57) filed on 29 April 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

1b. Applicants also elected the nucleic acid of SEQ ID NO:1, encoding the polypeptide of SEQ ID NO:2, with traverse. Initially, Applicants request clarification whether the restriction between the recited sequences is a requirement of an election of a genus of nucleic acid molecules encoding human, murine, or rat GPCR polypeptides. Applicants further submit that the nucleic acids of SEQ ID Nos: 1, 3 and 5 encode human, murine and rat GPCR polypeptides, respectively. Applicants submit that the human, rat and murine GPCR polypeptides share a high degree of similarity and also share common structural properties because they all possess 7 transmembrane domains. Thus, Applicants conclude that the members of this genus do not constitute multiple independent and distinct inventions, therefore, Applicants request that examination of claims directed to nucleic acid molecules encoding human, murine and rat GPCR polypeptides.

These grounds of traversal have been fully considered but are not deemed persuasive. First, the requirement to elect one single nucleic acid is not to be considered as a requirement of an election of species, since each of the

nucleic acids recited in alternative from is not a member of a single genus of invention, but constitutes an independent and patentably distinct invention, as explained below. Second, nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Although the polypeptides encoded by the recited nucleic acids share some similarity and may belong to the GPCR family of proteins, they are still distinct and different compounds, because the GPCR family of proteins bind to different ligands that possess diverse activities and play disparate physiological roles. Finally, a single search would not reveal art pertinent to all of the recited sequences. Thus, searching all of the recited nucleic acids would pose undue burden on the Examiner.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 9, 12-42, 46-55 and 58 are withdrawn from consideration by the Examiner as they are drawn to non-elected inventions.

Claim objections:

2a. Claims 1-8, 10-11, 43-45 and 56-57 are objected to because of the following informalities:

Claims 1-8, 10-11, 43-45 and 56-57 are objected to because they recite non-elected SEQ ID Nos.

Claims 4-8, 10-11, 43-45 and 56-57 are objected to, insofar as they depend on claims 1-3. Appropriate correction is required.

Claim rejections-35 USC § 101:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3a. Claims 1-8, 10-11, 43-45 and 56-57 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims of the instant invention are directed to a recombinant nucleic acid comprising a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:1, said nucleic acid encoding the polypeptide of SEQ ID NO:2. The specification describes the nucleic acid of SEQ ID NO:1 as human GPCR gene and the polypeptide of SEQ ID NO:2 as the deduced amino acid sequence of the human GPCR polypeptide, (see figures 1A and 1B). However, the instant specification does not disclose a ligand for the GPCR encoded by the claimed nucleic acid. Neither does the specification disclose an activity for said polypeptide.

Instant specification discloses that the GPCR polypeptide encoded by the claimed nucleic acid has been detected in the fat tissue, and asserts that the GPCR nucleic acid, the GPCR polypeptide and agonists, antagonists thereof

may be useful for the treatments or diagnosis involving fat metabolism. The specification list examples of diseases, including obesity, diabetes, dislipidemia, cachexia, AIDS, anorexia nervosa, among other disease that can be treated using the molecules of the instant invention, (see page 76, lines 14-30).

While the instant specification asserts that the GPCR encoded by the claimed nucleic acid can be used therapeutically, and discloses conventional protein and nucleic acid administration techniques, it does not disclose any specific disease ~~where~~ that said GPCR or the nucleic acid encoding it has actually been used to treat. Instant specification does not establish a connection between the claimed nucleic acid or the encoded polypeptide and a specific disease or disorder, but merely speculates that the claimed nucleic acid or the encoded polypeptide are useful for treating disparate diseases. Although the instant specification discloses that the GPCR polypeptide of the instant invention is expressed in fat tissue, it does not disclose information regarding a correlative or causal relationship between the expression of the claimed nucleic acid in said tissue and any of the listed diseases. Furthermore, the instant specification does not show how can the claimed nucleic acid or the encoded polypeptide be used in the detection of any disease, since it does not show that these molecules are only expressed in diseased tissues as compared to healthy tissues. Therefore, in the absence of any disclosed relationship between the claimed nucleic acid or the encoded polypeptide and any disease or disorder, one of ordinary skill in the art would not know how to use the claimed invention.

Thus, without knowing the specific ligand, or biological function for the GPCR polypeptide encoded by the claimed nucleic acid and which physiological processes that these molecules are involved in, a specific or substantial utility can not be established for said human GPCR polypeptide or the nucleic acid encoding it. The fact that the GPCR polypeptide is expressed in fat tissue is not enough to establish a specific or substantial utility for it, because there no nexus established between the claimed nucleic acid or the GPCR polypeptide encoded thereby and any disease or disorder.

3b. Claims 1-8, 10-11, 43-45 and 56-57 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The GPCR polypeptide encoded by the claimed nucleic acid has never been expressed, no biological activity was assayed or determined for it and no ligand was disclosed for it. Furthermore, Applicants have not disclosed the physiological role of the claimed nucleic acid or the encoded polypeptide nor have they established a nexus between the claimed nucleic acid or the encoded receptor and any disease or disorder.

Although the specification describes the structure of the nucleic acid molecule of SEQ ID NO:1 and the encoded human GPCR polypeptide as SEQ ID NO:2, it does not describe how to use said GPCR polypeptide or the claimed nucleic acid molecule encoding it. Therefore, there is no specific and substantial

asserted utility or well established for the claimed nucleic acid or the encoded GPCR polypeptide.

Even if Applicants establish an activity for the polypeptide of SEQ ID NO:2 encoded by the claimed nucleic acid, the instant specification would still fail to adequately enable an isolated nucleic acid which encoded a polypeptide which is at least 70% identical to the polypeptide of SEQ ID NO:2 which retains the polypeptide of SEQ ID NO:2, or an isolated nucleic acid which encodes a fragment of at least 25 amino acid residues, of SDEQ ID NO:2, which retains the activity of the polypeptide of SEQ ID NO:2. Neither does the specification enable an isolated nucleic acid with at least one conservative amino acid substitution, one amino acid insertion, one amino acid deletion, or which has a C-and/or N terminal truncation all of which retain the activity of the polypeptide of SEQ ID NO:2. For example, Applicants do not teach which 30% of the polypeptide of SEQ ID NO:2 to mutate, or which regions of the polypeptide of SEQ ID NO:2 can tolerate deletions, insertions or substitutions of at least one amino acid, without affecting the activity of said polypeptide. Applicants also do not teach a fragment of 25 amino acid residues of the polypeptide of SEQ ID NO:2 that retains the activity of the polypeptide. Thus without information regarding which regions of the polypeptide of SEQ ID NO:2 are critical to a specific function, the full scope of the claimed invention is not enabled.

In summary, the amount of experimentation required for one of ordinary skill in the art to make and use an isolated nucleic acid which encodes a polypeptide having 70% identity to SEQ ID NO:2, or an isolated nucleic acid

which encodes a fragment of at least 25 amino acid residues, of SEQ ID NO:2, which retains the activity of the polypeptide of SEQ ID NO:2 would be undue. In Ex parte Forman, 230 USPQ 546 (Bd. Pat. Appls, and Interf. 1986), the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims. In the instant application, Applicants only disclose one polypeptide, said polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, encoded by the claimed nucleic acid, and it will be undue experimentation to delineate "all" possible polypeptides that contain 70% identity to the polypeptide SEQ ID NO:2 which retain the desired activity, because Applicants have not taught which 104 amino acid residues of SEQ ID NO:2 to alter without altering the desired activity. Furthermore, the state of the art is such that it is acknowledged that amino acid modifications of proteins is unpredictable, thus one of ordinary skill in the art would not be able to predict which amino acids to delete or to substitute while still preserving the desired activity. Neither has the specification disclosed where of the polypeptide of SEQ ID NO:2 to insert amino acids without altering the desired activity. There is no upper limit as to how many amino acids to be substituted, deleted, or inserted or which regions of the

polypeptide are critical for its' function, the skilled artisan would not know how to make and use the claimed polypeptide.

The instant specification as filed also only describes the structure of the nucleic acid encoding the polypeptide of SEQ ID NO:2, and fails to describe nucleic acid molecules encoding: allelic variants, splice variants of the polypeptide of SEQ ID NO:2 or encoding a fragment of the polypeptide comprising 25 amino acid residues that the has the activity of the polypeptide of SEQ ID NO:2, or a nucleic acid that encodes a polypeptide that varies from the polypeptide of SEQ ID NO:2 by 30%, or which has a C-and/or N terminal truncation, that still retains the desired activity. Therefore, conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention.

To satisfy the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); Hyatt v. Boone, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998). Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. Adequate written description requires more than a mere statement that it is part of the invention. The court indicated that while Applicants are not required to disclose every

species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In the instant case, Applicants are claiming nucleic acids encoding variants and fragments of the polypeptide of SEQ ID NO:2 that still retain the desired activity, however, Applicants do not provide the structure of any said variants or fragments.

Therefore only the nucleic acid encoding the polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 U.S.C. § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-8, 10-11, 43-45 and 56-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 1, 2, 3 recite ".... Nucleotide that hbridizes under at least moderate stringent conditions....", however, this is a conditional term and renders the claims indefinite. This rejection could be obviated by supplying specific

conditions supported by the specification, which Applicants consider to be "moderate stringent".

4b. Claim 3 recites ".... With at least one amino acid deletion, substitution, insertion...", however it is unclear how many amino acids of the polypeptide of SEQ ID NO:2 to delete, insert or substitute for. There is no upper limit for how many amino acids to alter, is it only one, ten or more? The metes and bounds of the claim can not e ascertained.

Claims 4-8, 10-11, 43-45 and 56-57 are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, so long as they depend from claims 1, 2, or 3 for the limitations set forth directly above.

Claim rejections-35 USC § 102:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5a. Claims 1-8, 10-11, 43-45 and 56-57 are rejected under 35 U.S.C § 102(a) as being anticipated by (WO 01/36473 published May/2001; WO 01/36471 published May/2001, WO 73029 published Octobert/2001; WO 74904 published October/2001).

Each of these references teaches an isolated nucleic acid molecule comprising a nucleotide sequence that shares 100% identity to the instant nucleic acid of SEQ ID NO:1 and encodes a polypeptide that shares 100% identity to the polypeptide of SEQ ID NO:2 of the instant application. (See attached copy of the comparison of SEQ ID NO:2 of the instant invention and the sequences of the references (SEQUENCE COMPARISON 'A-D', respectively).

The references also teach a vector comprising said nucleic acid, a host cell comprising said vector, a method of producing the encoded polypeptide, a composition comprising said nucleic acid and a pharmaceutically acceptable carrier and a gene chip comprising said nucleic acid (see the claims of the references). Therefore each of the references anticipates the instant claims 1-8, 10-11, 43-45 and 56-57 in the absence of any evidence to the contrary.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647

12 July 2004

JANET ANDRES
PATENT EXAMINER